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OBSERVATIONS ON THE BACTERIOLOGY OF CHOREA

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The frequent association or sequence of tonsillitis, acute rheumatic fever, endocarditis, and chorea in children is an ancient observation in clinical medicine. The etiology of chorea has been explained on several theories, one of which is that it is an infection.

Many investigators have obtained bacteria in blood cultures in chorea before and after death, but in a large number of these cases, rheumatic fever or acute cardiac involvement was associated. There is very little written of the bacteriology of uncomplicated chorea.

Pianese¹ isolated a bacillus from a postmortem blood culture. Dana demonstrated microscopically a diplococcus in the meninges of a patient dead of chorea, and Westphall, Wassermann, and Malkoff² isolated diplococci from the brain in chorea.

Poynton and Payne³ examined 4 fatal cases of rheumatism, 3 of which had chorea at the time of death. Diplococci were cultivated from the pia mater in 3 cases, and from the brain in 1.

Donath⁴ isolated *Staphylococcus albus* from the blood in chorea after death.

In 2 patients, 1 of whom had endocarditis and decompensation, Richards⁵ isolated a coccus which grew in short chains, and produced green pin-point colonies on blood agar in 6-8 days.

Apert⁶ and Richter⁷ each isolated diplococcus from the blood of a patient who had chorea during life.

Camisa⁸ reports 9 cases, from 6 of which cultures of the blood gave cocci arranged in short chains and pairs, all having the same morphologic and cultural characteristics. All these cases, however, showed evidence of cardiac involvement.

Donath⁴ cultured the blood of 7 severe cases, and isolated *Staphylococcus albus* in 4, and *Staphylococcus aureus* in 1.

Morse and Floyd¹⁰ examined 31 blood cultures taken from 26 patients, and found a diphtheroid bacillus in 1, cocci growing in short chains in 2, and a green

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¹ La Riforma Med., 1891.

² Jour. Med. Sc., 1894, 107, p. 31.

³ Berl. klin. Wchnschr., 1899, 36, p. 638.

⁴ Lancet, 1905, 2, p. 1760.

⁵ Ztschr. f. d. ges. Neurol. u. Psychiat., O., 1910, 4, p. 91.

⁶ Jour. Am. Med. Assn., 1914, 62, p. 110.

⁷ Compt. Rend. Soc. de Biol., 1898, 5, p. 128.

⁸ West. Lancet, 1883, 12, p. 531.

⁹ Centralbl. f. Bakteriologie, I, O., 1910, 52, p. 99.

¹⁰ Am. Jour. Dis. Child., 1916, 12, p. 61.

producing long chain coccus in one culture from a patient who had a complicating endocarditis.

In one case Collins¹¹ isolated a coccus growing in pairs and short chains.

LaFetra¹² reports many blood cultures of chorea in Bellevue Hospital, New York, only 2 of which were positive, both yielding *Streptococcus viridans*.

Bartley¹³ reports 4 negative cultures in 4 marked cases, and Koplik¹⁴ reported many cases cultured with negative results.

A few observations on the bacteriology of the spinal fluid and central nervous system after death have been made; in practically all the cases diplococci were found. There is very little in the literature on the bacteriology of the cerebrospinal fluid in chorea during life.

Donath⁵ isolated *Staphylococcus aureus* in one case.

Collins¹¹ reported negative results in all the cases he examined, and Passini¹⁵ made observations on 5 patients with only negative results.

Morse and Floyd¹⁰ cultured the spinal fluid of 19 patients, with negative results in all instances.

As to the tonsils, suffice it to say that Dick and Rothstein¹⁶ isolated hemolytic streptococci from the throats of patients sick with chorea, and with one strain produced what seemed like chorea, in 12 hours, in a dog.

The results of animal experimentation appear to have been inconclusive. Only a few isolated experiments have been reported in which choreiform movements have been produced in animals. From observation of healthy rabbits and dogs, it may be concluded that only those animals that exhibit persistent and marked twitchings and tremors after injections may be considered as having any significance, because many normal young dogs and rabbits normally show irregular slight twitchings of the muscles of the limbs and face.

Pianese¹ produced tremor in dogs and rabbits by injection of cultures of the bacillus isolated from the blood of a case of chorea after death.

Poynton and Payne⁴ describe twitchings, arthritis, and endocarditis in rabbits injected intravenously with diplococci obtained from the cerebrospinal fluid of a patient who died of chorea and rheumatism.

Donath⁵ reported inconclusive results in animals injected with *Staphylococcus albus* and *aureus* obtained by blood culture of patients sick with chorea.

The experimental chorea described by Dick and Rothstein¹⁶ in the dog is noteworthy, but as yet a preliminary report only of their work is at hand.

With the improvements in the technic in blood and tissue cultures in the living, in the past two decades, a large amount of work has been described which indicates a close association between hitherto unobserved foci of infection and acute infectious processes in remote parts of the body. Rosenow¹⁷ and others have produced arthritis and endocarditis in rabbits by the intravenous injection of organisms obtained by culture of the tonsils, blood, and joints of patients with rheumatic

¹¹ Brit. Med. Jour., 1913, 1, p. 220.

¹² Arch. Pediat., 1915, 22, p. 135.

¹³ Ibid., p. 137.

¹⁴ Ibid., p. 561.

¹⁵ Wien. klin. Wchnschr., 1914, 27, p. 1363.

¹⁶ Jour. Am. Med. Assn., 1913, 61, p. 1376.

¹⁷ Jour. Infect. Dis., 1914, 14, p. 61.

fever or endocarditis. Inasmuch as chorea is frequently associated with, or follows these conditions, I undertook to make cultures from the tonsils, and whatever other foci were observed, and from the blood and cerebrospinal fluid of acute, subacute and chronic cases of chorea, care being exercised to select only patients showing no evidence of active heart or joint involvement.

All instruments were boiled 10 minutes, and used directly from the sterilizer rack. The skin was washed with ether, painted with tincture of iodine, and allowed to dry. The blood was drawn from the median basilic vein, and transferred, after removal of the needle, to citrate solution, and inoculated within 15 minutes.

The spinal fluid was allowed to flow through the ordinary spinal puncture needle into sterile tubes, the end of the needle being flamed after removal of the obturator, and before collection of the fluid. In this case also cultures were made within 15 minutes.

Inoculations of the blood and cerebrospinal fluid were made in bottles of dextrose broth, anaerobic and aerobic tubes of ascitic dextrose broth, ascitic fluid rabbit kidney medium with paraffin oil layer, ascitic dextrose agar, ascitic dextrose blood-agar shake tubes, and blood-agar plates. Cultures were incubated at 37 C. for 10 days, and studied at intervals.

Material expressed from the tonsils, or swabs of the throat were streaked and plated on blood agar and kept under anaerobic and aerobic conditions.

Blood cultures were made in 21 patients, 10 of whom gave positive results. Nine gave small cocci, slightly elongated and arranged in pairs, short chains, and a few groups, in aerobic cultures. One only was strictly anaerobic. In 3 instances subcultures were sterile. Forty-eight hour broth cultures were slightly turbid, and there was a scant fine white sediment. On blood agar (10% goat blood) growth occurred in 1-4 days as fine colorless pin-point moist colonies. Two produced green about the colonies. None were hemolytic. Two strains grew in gelatin as very fine whitish colonies; the gelatin was not liquefied. In milk, 2 produced acid, but did not cause coagulation.

Of 6 strains of the cocci examined, all fermented dextrose and maltose, 5 fermented saccharose and lactose, 4 fermented mannite, 1 inulin, 1 raffinose, and 1 salicin.

The other positive blood culture gave a gram-positive short diphtheroid organism.

The cerebrospinal fluid of 21 patients has been cultured, with 13 positive results. One was not subcultured. Eight of the organisms isolated resembled very closely the organisms found in the blood. They were small, slightly elongated cocci, growing in pairs, short chains, and groups. Their growth on blood agar, gelatin, and in fluid mediums,

and their fermentation reactions, were in all respects similar to those of the cocci from the blood.

The other 5 organisms grew more luxuriantly in broth. Groups predominated, but there were a few in pairs, and a few short chains. On blood agar the colonies were larger, white, and more luxuriant after 24 hours. Their fermentative reactions were similar to those previously described.

Of 12 strains from the spinal fluid examined, all fermented dextrose, 11 maltose, 10 lactose, 9 saccharose, 3 mannite, 1 raffinose, and 1 inulin.

Throat cultures were made in 15 patients, and 29 cultures were isolated and studied.

Ten were hemolytic streptococci of variable size, occurring in long and short chains. Fermentation tests of 6 strains showed that all fermented raffinose and inulin, and 4 fermented saccharose.

Thirteen were green producing cocci, growing in pairs and short chains. Of 7 strains studied, all fermented raffinose, 6 inulin, 5 saccharose, and 3 dextrose.

Six were organisms which grew on blood agar as pin-point colorless nonhemolytic colonies, and resembled the organisms recovered from the blood in their morphologic and cultural characteristics, with the exception of their fermentative reactions. All fermented raffinose, 5 inulin, 3 saccharose, 3 dextrose, and 1 maltose.

The cases of chorea studied varied in duration from 10 days to 7 years, and in intensity from children who exhibited only mild choreiform movements in excitement to those so severe as to require restraint and feeding.

Those patients who yielded positive blood cultures had been ill from 10 days to 4 weeks; some, however, had recurring attacks.

Those yielding positive cultures from the cerebrospinal fluid had been sick from 10 days to 4 weeks, with the exception of one patient who had been ill 8 months.

Eleven patients gave histories of acute tonsillitis, two of rheumatism, and one of endocarditis. Eight gave no history of rheumatism, endocarditis, or tonsillitis.

A series of 25 rabbits were injected intravenously with various strains of organisms obtained from the tonsils, blood and spinal fluid. In no case were unmistakable persistent choreiform twitchings noted. In 2 rabbits there was some twitching of the forelegs and face 2 days and 12 hours, respectively, before death. A few animals succumbed in 24 hours, several in 5-7 days, and many

appeared unaffected. Postmortem examinations showed slight hyperemia of the meninges and brain in a few instances, and endocarditis in one. Cultures of the blood and spinal fluid did not consistently yield the organism injected.

One young dog was injected intravenously twice, the interval being 7 days, with an organism obtained from the cerebrospinal fluid of a marked case of chorea. No change was noted.

RESULTS OF EXAMINATION OF THE CEREBROSPINAL FLUID

There are many reports, chiefly French, of the cell count in the spinal fluid of patients ill with chorea. The majority of investigators have found a lymphocytosis.

Morse and Floyd¹⁰ examined the fluid in 10 instances and report a lymphocytosis in 3.

Twenty-one spinal fluids were examined in this study, and cell counts made within 15 minutes after withdrawal of the fluid.

Number of Cases	Cells per Cubic Millimeter
5	3
3	6
3	4
3	2
2	5
2	0
1	1
1	7
1	10

The average count was 3-6 cells. There was no constant relation between the severity of the chorea, the cultural results, and the cell count of the spinal fluid.

In all cases the tests for globulin carried out according to the technic of Nonne and Noguchi gave negative results.

Twelve of the 21 spinal fluids were tested for a reducing agent. All decolorized Fehling's solution, and produced a fine brick-red precipitate.

Wassermann tests with 3 antigens were negative in all cases.

SUMMARY

From so small a series of cases no general conclusions may be drawn. It is of interest that in 21 patients with chorea in public institutions none gave any evidence of syphilis, which consequently seems not to be of any etiologic importance in the disease.

TABLE 2
SUMMARY OF CASES

Number of Case, Sex and Age	Duration of Illness	Character of Attack	Cultures of Blood	Cultures of Cerebrospinal Fluid	Cultures of Tonsils	Previous Disease	Source
1—F 13	2 months	Very mild	No growth	Cocci, many	Hemolytic streptococci; green producing cocci; diplococci	Tonsillitis, rheuma- tism, endocarditis	Cook County Hos- pital
2—F 12	Irregularly, 4 years	Mild	Few diplococci	No growth	Hemolytic streptococci; green producing cocci	Tonsillitis	Cook County Hos- pital
3—M 8	2 weeks	Mild	No growth	No growth	Green producing cocci	Cook County Hos- pital
4—F 11	2 weeks	Very severe	Diplococci, many	Diplococci, many	Hemolytic streptococci; green producing cocci; diplococci	Tonsillitis	Cook County Hos- pital
5—M 9	3 weeks	Severe	Diplococci, few	Cocci, many	Hemolytic streptococci; diplo- cocci	Tonsillitis	Cook County Hos- pital
6—F 21	3 weeks	Mild	No growth	No growth	Green producing cocci; diplo- cocci	Rheumatism	Cook County Hos- pital
7—F 13	4 weeks	Very mild	No growth	No growth	Hemolytic streptococci; green producing cocci; diplococci	Tonsillitis	Cook County Hos- pital
8—F 11	2 weeks	Severe	No growth	No growth	Green producing cocci; hemo- lytic streptococci	Tonsillitis	Cook County Hos- pital
9—F 9	4 weeks	Severe	Diplococci, few	Diplococci, many	Hemolytic streptococci; diplo- cocci	Tonsillitis	Cook County Hos- pital
10—M 9	6 weeks	Very mild	Diplococci, few	Diplococci, few	Green producing cocci	Cook County Hos- pital
11—F 8	7 weeks	Very mild	Diplococci, few	Cocci, many	Green producing cocci; hemo- lytic streptococci	Tonsillitis	Cook County Hos- pital
12—F 6	2 weeks	Severe	No growth	Diplococci, few	Tonsillitis	Cook County Hos- pital
13—F 12	4 months	Mild	No growth	Cocci, many	Tonsillitis	Childrens' Memo- rial Hospital
14—M 11	3 weeks	Very mild	Diplococci, few	Cocci, many	Childrens' Memo- rial Hospital
15—F 8	1 week	Severe	Diplococci, few	Cocci, many	Cook County Hos- pital
16—M 1/	2 weeks	Very severe	No growth	Diplococci, few	Cook County Hos- pital
17—M 14	4 weeks	Severe	Diphtheroid organism	Diplococci, few	Cook County Hos- pital
18—F 19	2 years	Mild	No growth	No growth	Tonsillitis	Cook County Hos- pital
19—M 10	2 weeks	Severe	Diplococci, few	Diplococci, few	Hemolytic streptococci; green producing cocci	Cook County Hos- pital
20—F 9	4 weeks	Mild	No growth	No growth	Hemolytic streptococci; green producing cocci	Childrens' Memo- rial Hospital
21—F 21	4 months	Severe	No growth	No growth	Green producing cocci	Cook County Hos- pital

There is nothing characteristic or peculiar in the spinal fluid of chorea. Accepting the presence of globulin in the spinal fluid, and an increase in the number of cells, as indication of irritation or inflammation of the meninges, these results indicate that there are no changes in the meninges in chorea as a rule.

Of 21 cases, 10 yielded positive cultures from both the blood and spinal fluid, and 14 in either one or the other. Six of the bacterial strains isolated from the tonsil, 8 from the spinal fluid, and 9 from the blood, were identical in their morphologic and cultural characteristics. It therefore seems that bacteria are of importance in chorea and that the coccus mentioned in the foregoing is most frequently present, judging from the results in this series as well as the work of others.

As to the grouping of the organism, its slow, scant, pin-point growth on blood agar, the slight turbidity and fine granular sediment produced in broth, would seem to relate it with the streptococci. In the predominance of pairs, with few short chains, and a few irregular groups, when grown in broth, it resembles the streptococci also, and especially the streptococci or diplococci frequently found in rheumatic fever and endocarditis. It should be noted that the strains studied do not as a rule cause hemolysis on blood-agar plates. No definite grouping can be made on the basis of the fermentative reactions as observed.

So far experiments on animals with this coccus, which is being studied further, have been inconclusive.